REMARKS

This is intended as a full and complete response to the Office Action dated January 4, 2006, having a shortened statutory period for response set to expire on April 4, 2006. Please reconsider the claims pending in the application for reasons discussed below.

Claims 19-32 remain pending in the application and are shown above. Claims 19-32 stand rejected. Reconsideration of the rejected claims is requested for reasons presented below.

Claims 19-32 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over *Ketcham et al.* (U.S. Patent No. 4,871,489) in view of *Backstrom et al.* (U.S. Patent No. 5,952,008) and *Forrester et al.* (U.S. Patent No. 4,590,489). Applicant respectfully traverses the rejection.

Ketcham discloses an apparatus for producing liquid droplets of solutions of metal oxides or metal oxide precursors such as zirconium hydroxynitrate, zirconium acetate, aluminum oxide, and aluminum hydroxynitrate. The solutions are fed through a feed tube 11 and through an orifice plate 13 (See, Figure 1 and column 3, lines 59-67.) The orifice plate is connected to an orifice cup 14 which is in active engagement with a vibratory element 15. The vibratory element 15 causes the orifice plate to vibrate and is located away from the flow of the liquid feed. Thus, in *Ketcham*, the liquid feed is forced into an area defined by feed tube 11 and orifice plate 13.

Backstrom teaches that active compounds should consist of particles having a diameter less than approximately 10 μm (e.g., between 0.01-10 μm, and ideally between 1-6 μm). In preferred embodiments, at least 50% (preferably at least 60%, more preferably at least 70%, still more preferably at least 80%, and most preferably at least 90%) of the total mass of the active compounds consists of particles within the desired diameter range. However, in examples of micronized active compounds the mass median diameters are in the range of 2.4 μm to 9.6 μm, depending on the samples used. The examples do not disclose any particle size distribution data. Similarly, *Forrester* prefers that the particles be at least 50% by weight and preferably more than 90%, of the particles of the active compound be less than 60 μm, and

especially less than 10 μm in diameter. *Forrester* particularly prefers at least 50 % of the particles to be of 2 to 6 in diameter. However, in the only example of small particle sizes, an average mass mean diameter of 11 μm was obtained. (See column 15, lines 65-66.)

Pending claim 19 recites forcing the liquid feed stock into a manifold defined between a vibratable element and a plate and forcing the feedstock through the plate. Because the vibratable element of *Ketcham* is located away from the flow of the liquid feed, the combination of *Ketcham* with *Backstrom* and *forrester* does not teach, show or suggest forcing the liquid feed stock into a manifold defined between a vibratable element and a plate, as recited in claim 19.

Furthermore, *Ketcham* does not suggest producing particles of pharmaceutical compounds. *Backstrom* teaches pharmaceutical compositions which are micronized in order to make them suitable for inhalation. The miconization is performed in a suitable mill, such as a jet mill (column 8, lines 34-36), and does not involve the formation of droplets which are dried by a drying gas. There is no suggestion in the combination of *Ketcham*, *Backstrom*, and *Forrester* that the active pharmaceutical compounds of *Backstrom* and *Forrester* will form particles with the narrow size distributions as recited in *Ketcham* and claims 19 and 32.

Therefore, the combination of *Ketcham*, *Backstrom*, and *Forrester* does not teach, show, or suggest a method for spray drying a feed stock containing a pharmaceutical agent to produce particles suitable for pulmonary administration having a narrow particle size distribution comprising: providing a liquid feed stock comprising a pharmaceutically active agent selected from the group consisting of insulin, calcitonin, erythropoietin (EPO), Factor VIII, Factor IX, ceredase, cerezyme, cyclosporine, granulocyte colony stimulating factor (GCSF), alpha-1 proteinase inhibitor, elcatonin, granulocyte macrophage colony stimulating factor (GMCSF), growth hormone, human growth hormone (HGH), growth hormone releasing hormone (GHRH), heparin, low molecular weight heparin (LMWH), interferon alpha, interferon beta, interferon gamma, interleukin-2, luteinizing hormone releasing hormone (LHRH), somatostatin, octreotide, vasopressin analog, follicle stimulating hormone (FSH), insulin-like growth factor, insulintropin, interleukin-1 receptor antagonist, interleukin-3,

interleukin-4, interleukin-6, macrophage colony stimulating factor (M-CSF), nerve growth factor, parathyroid hormone (PTH), thymosin alpha 1, IIb/IIIa inhibitor, alpha-1 antitrypsin, respiratory syncytial virus antibody, cystic fibrosis transmembrane regulator (CFTR) gene, deoxyribonuclease (Dnase), bactericidal/permeability increasing protein (BPI), anti-CMV antibody, interleukin-1 receptor, 13-cis retinoic acid, pentamidine isethionate, albuterol sulfate, metaproterenol sulfate, beclomethasone dipropionate, triamcinolone acetamide, budesonide acetonide, ipratropium bromide, flunisolide, fluticasone, cromolyn sodium, and ergotamine tartrate; forcing said liquid feed stock into a manifold defined between a vibratable element and a plate and forcing the feed stock through the plate, said plate comprising holes of at least one predetermined diameter, in order to produce liquid droplets; drying said droplets in a gas stream to produce dried particles comprising a mass median aerodynamic diameter of less than 10 microns and a particle size distribution wherein at least 70% of the mass of the particles have a diameter within a 4 micron range; and collecting said dried particles, as recited by claim 19. Withdrawal of the rejection is respectfully requested.

Furthermore, the combination of *Ketcham*, *Backstrom*, and *Forrester* does not teach, show, or suggest a method for spray drying a feed stock containing a pharmaceutical agent comprising: providing a liquid feed stock comprising a pharmaceutically active agent selected from the group consisting of insulin, calcitonin, erythropoietin (EPO), Factor VIII, Factor IX, ceredase, cerezyme, cyclosporine, granulocyte colony stimulating factor (GCSF), alpha-1 proteinase inhibitor, elcatonin, granulocyte macrophage colony stimulating factor (GMCSF), growth hormone, human growth hormone (HGH), growth hormone releasing hormone (GHRH), heparin, low molecular weight heparin (LMWH), interferon alpha, interferon beta, interferon gamma, interleukin-2, luteinizing hormone releasing hormone (LHRH), somatostatin, octreotide, vasopressin analog, follicle stimulating hormone (FSH), insulin-like growth factor, insulintropin, interleukin-1 receptor antagonist, interleukin-3, interleukin-4, interleukin-6, macrophage colony stimulating factor (M-CSF), nerve growth factor, parathyroid hormone (PTH), thymosin alpha 1, IIb/IIIa inhibitor, alpha-1 antitrypsin, respiratory syncytial virus antibody, cystic fibrosis transmembrane regulator (CFTR)

gene, deoxyribonuclease (Dnase), bactericidal/permeability increasing protein (BPI), anti-CMV antibody, interleukin-1 receptor, 13-cis retinoic acid, pentamidine isethionate, albuterol sulfate, metaproterenol sulfate, beclomethasone dipropionate, triamcinolone acetamide, budesonide acetonide, ipratropium bromide, flunisolide, fluticasone, cromolyn sodium, and ergotamine tartrate; atomizing said feed stock in order to produce liquid droplets; drying said droplets in a gas stream to produce dried particles comprising a mass median aerodynamic diameter of less than 10 microns and particle size distribution wherein at least 70% of the mass of the particles have a diameter within a 4 micron range; and collecting said dried particles, as recited by claim 32. Withdrawal of the rejection is respectfully requested.

In conclusion, the references cited by the Examiner, alone or in combination, do not teach, show, or suggest the invention as claimed.

Having addressed all issues set out in the office action, Applicant respectfully submits that the claims are in condition for allowance and respectfully request that the claims be allowed.

Respectfully submitted,

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